Amendments to the Claims

Please amend the claims as follows:

1. (Currently amended): A process of ~~making a genetically engineered neisserial strain with an L2 or L3 LOS immunotype of reduced phase variability for manufacture of an immunogenic composition~~ isolating L3 LOS comprising the steps of:

a) selecting a neisserial strain with phase-variable L3 LOS synthesis,

b) genetically engineering the strain such that the homopolymeric nucleotide tract of a phase-variable lgtA ~~and/or lgtG~~ LOS oligosaccharide synthesis gene is modified to render the expression of the gene less phase variable, and

c) isolating ~~L2 or~~ L3 LOS from the neisserial strain~~, and~~

~~d) formulating the isolated L2 or L3 LOS with a pharmaceutically acceptable excipient~~.

2. (Currently amended): The process of claim 1, wherein the L3 LOS oligosaccharide synthesis gene is modified to render the expression of the gene non-phase variable.

3. (Previously presented): The process of claim 1, wherein the genetically engineered neisserial strain made has an LOS immunotype that is non-phase variable.

4. (Previously presented): The process of claim 1, wherein the neisserial strain is selected from the group of a meningococcal strain and a meningococcus B strain.

5. (Previously presented): The process of claim 1, wherein the genetically engineered neisserial strain made has L2 LOS immunotype.

6. (Previously presented): The process of claim 5, wherein step a) a neisserial strain with phase-variable L2 LOS synthesis is selected.

7. (Previously presented): The process of claim 5, wherein step b) comprises the step of fixing expression of an IgtA gene product.

8. (Previously presented): The process of claim 7, wherein the expression of an IgtA gene product is fixed by reducing the length of the homopolymeric nucleotide tract within the open-reading frame of the gene and maintaining the open-reading frame in frame.

9. (Previously presented): The process of claim 8, wherein the homopolymeric G tract in the IgtA open-reading frame is reduced to 8, 5 or 2 consecutive G nucleotides.

10. (Previously presented): The process of claim 7, wherein the expression of an IgtA gene product is fixed by changing the sequence of the homopolymeric G nucleotide tract within the open-reading frame of the IgtA gene such that: one or more GGG codons encoding Glycine is changed to any other codon encoding Glycine, or a codon encoding a conservative mutation, and/or the TCG codon encoding Serine is changed to any other codon encoding Serine, or a codon encoding a conservative mutation, and maintaining the open-reading frame of the gene in frame.

11. (Previously presented): The process of claim 10, wherein 2, 3 or 4 codons in the homopolymeric tract are changed and encode the identical amino acid or a different amino acid.

12. (Previously presented): The process of claim 5, wherein step b) comprises the step of fixing the expression of an IgtG gene product.

13. (Previously presented): The process of claim 12, wherein the expression of an IgtG gene product is fixed by reducing the length of the homopolymeric

nucleotide tract within the open-reading frame of the gene and maintaining the open-reading frame in frame.

14. (Previously presented): The process of claim 13, wherein the homopolymeric C tract in the IgtG open-reading frame is reduced to 8, 5 or 2 consecutive C nucleotides.

15. (Previously presented): The process of claim 12, wherein the expression of an IgtG gene product is fixed by changing the sequence of the homopolymeric C nucleotide tract within the open-reading frame of the IgtG gene such that: one or more CCC codons encoding Proline is changed to any other codon encoding Proline, or a codon encoding a conservative mutation, or the GCC codon encoding Alanine is changed to any other codon encoding Alanine, or a codon encoding a conservative mutation, and maintaining the open-reading frame in frame.

16. (Previously presented): The process of claim 15, wherein 2, 3 or 4 codons in the homopolymeric tract are changed and encode the identical amino acid or a different amino acid.

17. (Previously presented): The process of claim 5, wherein step b) comprises the steps of (1) fixing the expression of an IgtA gene product by reducing the length of the homopolymeric G nucleotide tract within the open-reading frame of the gene to 5 or 2 consecutive G nucleotides and maintaining the open-reading frame in frame or optionally changing the sequence of the homopolymeric G nucleotide tract such that one or more GGG codons encoding Glycine is changed to any other codon encoding glycine, or a codon encoding a conservative mutation, or the TCG codon encoding Serine is changed to any other codon encoding Serine, or a codon encoding a conservative mutation, and maintaining the open-reading frame of the gene in frame, and (2) fixing the expression of an IgtG gene product by changing the sequence of the homopolymeric C nucleotide tract within the open-reading frame of the IgtG gene such that 1, 2 or 3 CCC codons encoding Proline is changed to any

other codon encoding Proline, or a codon encoding a conservative mutation, or the GCC codon encoding Alanine is changed to any other codon encoding Alanine, or a codon encoding a conservative mutation, whilst maintaining the open-reading frame in frame.

18. (Cancelled)

19. (Cancelled)

20. (Currently amended): The process of ~~claim 18 or 19~~ claim 1, wherein step b) comprises the step of fixing the expression of an ~~IgtA~~ lgtA gene product.

21. (Currently amended): The process of claim 20, wherein the expression of the ~~IgtA~~ lgtA gene product is fixed by reducing the length of the homopolymeric nucleotide tract within the open-reading frame of the gene and maintaining the open-reading frame in frame.

22. (Currently amended): The process of claim 21, wherein the homopolymeric G tract in the ~~IgtA~~ lgtA open-reading frame is reduced to 8, 5 or 2 consecutive G nucleotides.

23. (Currently amended): The process of claim 20, wherein the expression of an IgtA gene product is fixed by changing the sequence of the homopolymeric G nucleotide tract within the open-reading frame of the ~~IgtA~~ lgtA gene such that one or more GGG codons encoding Glycine is changed to any other codon encoding glycine, or a codon encoding a conservative mutation, or the TCG codon encoding Serine is changed to any other codon encoding Serine, or a codon encoding a conservative mutation and maintaining the open-reading frame of the gene in frame.

24. (Previously presented): The process of claim 23, wherein 2, 3 or 4 codons in the homopolymeric tract are changed and encode the identical amino acid or a different amino acid.

25. (Currently amended): The process of ~~claim 18~~ claim 1, wherein step b) comprises the step of permanently downregulating the expression of a gene product from the ~~IgtG~~ lgtG gene.

26. (Currently amended): The process of claim 25, wherein the expression of the gene product from the ~~IgtG~~ lgtG gene is switched off, optionally by deleting all or part of the promoter or open-reading frame of the gene.

27. (Currently amended): The process of ~~claim 18~~ claim 1, wherein step b) comprises the steps of fixing the expression of the ~~IgtA~~ lgtA gene product by reducing the length of the homopolymeric G nucleotide tract within the open-reading frame of the gene to 2 consecutive G nucleotides and maintaining the open-reading frame in frame, and switching off the expression of gene product from the ~~IgtG~~ lgtG gene by deleting all or part of the promoter or open-reading frame of the gene.

28. (Currently amended): The process of ~~claim 5~~ claim 1, wherein step b) further comprises the step of permanently downregulating the expression of gene product from the ~~IgtC~~ lgtC gene, optionally by switching the gene off or by deleting all or part of the promoter or open-reading frame of the gene.

29. (Currently amended): The process of ~~claim 5~~ claim 1, wherein step a) further comprises the step of selecting a neisserial strain that is ~~IgtB~~ lgtB$^-$, or step b) further comprises the step of genetically engineering the strain such that the expression of gene product from the ~~IgtB~~ lgtB or ~~IgtE~~ lgtE gene is permanently downregulated, optionally by switching the gene off or by deleting all or part of the promoter or open-reading frame.

30. (Currently amended): The process of ~~claim 5~~ claim 1, wherein step a) further comprises the step of selecting a neisserial strain that is unable to synthesise capsular polysaccharide, or step b) further comprises the step of genetically engineering the strain such that it is unable to synthesize capsular polysaccharide by permanently downregulating the expression of gene product from one of the following genes: ~~saiD~~ siaD, ctrA, ctrB, ctrC, ctrD, synA, synB or synC, optionally by switching the gene off or by deleting all or part of the promoter or open-reading frame.

31. (Currently amended): The process of ~~claim 5~~ claim 1, wherein step a) further comprises the step of selecting a neisserial strain that is msbB- or htrB-, or step b) further comprises the step of genetically engineering the strain such that the expression of functional gene product from the msbB or htrB gene(s) is permanently downregulated, optionally by switching the gene(s) off or by deleting all or part of the promoter or open-reading frame.

32. (Previously presented): A process of isolating L2 LOS comprising the steps of producing a genetically engineered neisserial strain with a fixed L2 immunotype by the process of claim 5 or 28; and isolating L2 LOS from the resulting strain.

33. (Previously presented): The process of claim 32, comprising the step of conjugating the L2 LOS to a carrier comprising a source of T-cell epitopes or the step of presenting the L2 LOS in a liposome formulation.

34. (Previously presented): A process of isolating neisserial blebs having an L2 LOS immunotype, comprising the steps of producing a genetically engineered neisserial strain with a fixed L2 immunotype by the process of claim 5 or 28; and isolating blebs from the resulting strain.

35. (Previously presented): The process of claim 34, where the step of isolating blebs involves extraction with about 0.03%, about 0.05-0.2% or about or exactly 0.1% deoxycholate.

36. (Previously presented): The process of claim 34, comprising the step of intra-bleb conjugating the L2 LOS to an outer membrane protein present in the blebs.

37. (Cancelled)

38. (Currently amended): The process of ~~claim 37~~ claim 1, further comprising the step of conjugating the L3 LOS to a carrier comprising a source of T-cell epitopes or the step of presenting the L3 LOS in a liposome formulation.

39. (Previously presented): A process of isolating neisserial blebs having an L3 LOS immunotype, comprising the steps of producing a genetically engineered neisserial strain with a fixed L3 immunotype by the process of claim 18; and isolating blebs from the strain.

40. (Previously presented): The process of claim 39, where the step of isolating blebs involves extraction with about 0.03%, about 0.05-0.2%, or about or exactly 0.1% deoxycholate.

41. (Previously presented): The process of claim 39, comprising the step of intra-bleb conjugating the L3 LOS to an outer membrane protein present in the blebs.

42. (Previously presented): A process of making an immunogenic composition comprising the steps of producing isolated L2 LOS by the process of claim 32 and formulating the L2 LOS with a pharmaceutically-acceptable excipient.

43. (Previously presented): A process of making an immunogenic composition comprising the steps of producing isolated L3 LOS by the process of claim 37 and formulating the L3 LOS with a pharmaceutically acceptable excipient.

44. (Previously presented): A process of making a multivalent immunogenic composition comprising the steps of producing isolated L2 LOS by the process of claim 32 or producing isolated neisserial blebs having an L2 LOS immunotype, producing isolated L3 LOS or producing isolated neisserial blebs having an L3 LOS immunotype and mixing the L2 and L3 LOS components together along with a pharmaceutically acceptable excipient.

45. (Currently amended): A process of growing a high cell density of an ~~L2 or~~ L3 neisserial strain comprising the steps of:
a) genetically-engineering a neisserial strain according to ~~claim 5~~ claim 1;
b) growing the strain to high cell density in a fermentor.

46. (Previously presented): The process of claim 45, wherein the strain is grown to a cell density in iron non-limiting conditions of OD_{450} 10-19, or OD_{450} 12-16 or is grown to a cell density in iron limiting conditions of OD_{450} 6-12 or OD_{450} 8-10.

47. (Currently amended): A process of isolating neisserial ~~L2 or~~ L3 LOS comprising the steps of growing an ~~L2 or~~ L3 neisserial strain to high cell density according to the process of claim 45, and isolating ~~L2 or~~ L3 LOS from the resulting strain.

48. (Currently amended): The process of claim 47, comprising the step of conjugating the ~~L2 or~~ L3 LOS to a carrier comprising a source of T-cell epitopes or the step of presenting the ~~L2 or~~ L3 LOS in a liposome formulation.

49. (Previously presented): A process of isolating neisserial blebs having an L2 or L3 LOS immunotype, comprising the steps of growing an L2 or L3 neisserial strain to high cell density according to the process of claim 45; and isolating blebs from the resulting strain.

50. (Previously presented): The process of claim 49, where the step of isolating blebs involves extraction with about 0-0.3%, about 0.05-0.2%, or about or exactly 0.1% deoxycholate.

51. (Previously presented): The process of claim 49, comprising the step of intra-bleb conjugating the L2 or L3 LOS to an outer membrane protein also present in the blebs.

52. (Previously presented): A process of making an immunogenic composition comprising the steps of producing isolated L2 or L3 LOS by the process of claim 47 or producing isolated neisserial blebs having an L2 or L3 LOS immunotype and formulating the L2 or L3 LOS or blebs with a pharmaceutically acceptable excipient.

53. (Previously presented): A process of making an immunogenic composition comprising the steps of producing isolated L2 LOS by the process of claim 47 or producing isolated neisserial blebs having an L2 LOS immunotype, producing isolated L3 LOS and mixing the L2 and L3 LOS components together along with a pharmaceutically acceptable excipient.

54. (Previously presented): A process of making an immunogenic composition comprising the steps of producing isolated neisserial blebs having an L2 LOS immunotype by the process of claim 35, and formulating the L2 LOS or blebs with a pharmaceutically-acceptable excipient.

55. (Previously presented): A process of making an immunogenic composition comprising the steps of producing isolated L3 LOS by the process of claims 39, and formulating the L3 LOS or blebs with a pharmaceutically acceptable excipient.

56. (Previously presented): A process of making an immunogenic composition comprising the steps of producing isolated neisserial blebs having an L2 LOS immunotype by the process of claims 34, and mixing the L2 LOS or blebs with a pharmaceutically acceptable excipient.

57. (Previously presented): A process of making an immunogenic composition comprising the steps of producing isolated neisserial blebs having an L3 LOS immunotype by the process of claim 39, and mixing the L3 LOS or blebs with a pharmaceutically acceptable excipient.

58. (Previously presented): A process of making an immunogenic composition comprising the steps of producing isolated neisserial blebs having an L2 or L3 LOS immunotype by the process of claim 49, and formulating the L2 or L3 LOS or blebs with a pharmaceutically acceptable excipient.

59. (Previously presented): A process of making an immunogenic composition comprising the steps of producing isolated neisserial blebs having an L2 LOS immunotype by the process of claim 49, and mixing the L2 LOS or blebs and a pharmaceutically acceptable excipient.

60. (Previously presented): A process of making an immunogenic composition comprising the steps of producing isolated neisserial blebs having an L3 LOS immunotype by the process of claim 49, and mixing the L3 LOS or blebs with a pharmaceutically acceptable excipient.